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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,792	04/13/2001	Robert F. Margolskee	AP32911 070165.0589	8395

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EXAMINER	
TURNER, SHARON L	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/834,792	MARGOLSKEE ET AL.	
	Examiner	Art Unit	
	Sharon L. Turner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *1-16, 18-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-23* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 November 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-23 are pending.

Priority

2. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

If applicant desires priority under 35 U.S.C 119(e) based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The Examiner notes that that the TRP8 molecule of SEQ ID NO:4 differs at residues 657, 990 and 1150 between the 60/197,491 provisional application and instant application. Further, the Examiner notes the rejection set forth below with respect to 35 USC 112, first paragraph. Thus, the disclosure of the invention within the provisional is not sufficient to comply with the requirements of the first paragraph of 35 USC 112 because priority to the TRP8 molecule is not apparently supported within the provisional application. Thus, for the purposes of examination the effective filing date of instant claims is the filing date of instant application, 4-13-01. Prior art is cited accordingly. Traversal should include a detailed reference to where support for the instantly claimed invention may be found within the provisional application and a discussion of how Applicant's view the provisional to support the claim recitations with respect to 35 USC 112, first paragraph for all limitations of the claims.

Drawings

3. The drawings are objected to because the requirements for color drawings have not been fulfilled as set forth below. A proposed drawing correction, corrected drawings or proper compliance with the requirements for color drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

4. Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the

color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the U.S. Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied. The Examiner notes that Figures 9, 12, and 13 are in color.

Election/Restriction

5. Applicant's election with traverse of Group IV, to the extent of human TRP8 of SEQ ID NO:4, claim 17 in Paper No. 14 submitted 3-24-03, is acknowledged. The traversal is on the ground(s) that the claimed processes of Groups I-X are not independent and distinct as required by 35 USC 121. This is not found persuasive because as set forth in the restriction requirement of 2-25-03 the products and methods are distinct as claimed and directed to divergent compounds, steps, effects and outcomes. A search for any one product or method is not co-extensive with any other and search and examination of the multiple groups in a single application bears undue burden upon the Examiner.

The requirement is still deemed proper and is therefore made FINAL.

6. Claims 1-16, and 18-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable

generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 14.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification describes polypeptide sequences consisting of SEQ ID NO:2 and 4 identified as human and mouse TRP8. The peptides are shown to have calcium channel activity as exhibited in Example 6.2.5, at p. 42 of the specification. The peptides are expressed in taste receptor cells and are disclosed as regulators of taste perception.

However, claim 17 as written recites "TRP8" generically and "TRP8 activation". Such recitations include multiple polypeptide variants comprising homologues from different species that vary substantially in length and also in amino acid sequence. The disclosure of SEQ ID NO:2 and SEQ ID NO:4 with the instantly disclosed acitivities, does not adequately support the scope of the claimed genus, which encompasses a

substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. However, the instant specification discloses only SEQ ID NO: 2 and SEQ ID NO:4 that share approximately 83% similarity.

The claims are neither directed to the representative sequences nor to the structural or functional features common to the genus. Moreover, the artisan has no guidance from the prior art as to that which constitutes "TRP8". Given the unpredictability of homology comparisons, and the fact that the specification fails to provide objective evidence of those sequences that constitute "TRP8" molecules, it cannot be established that a representative number of species have been disclosed to support the genus claim where no limitations other than the generic name are provided. No requisite activity is claimed for the TRP8 molecules and the specification cannot be read into the claims. Thus, for the aforementioned reasons, the claim lacks adequate written description support for "TRP8" and "TRP8 activation".

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 recites "the TRP8 channel protein" and "measuring the level" of "TRP8 activation". Yet the artisan cannot discern the metes and bounds of the "TRP8" molecules encompassed or the activities or measurements required to assess "the level of TRP8 activation." The molecule is not recognized in the prior art and there is no definitive activity or means of measurement noted by which the artisan can discern that encompassed by the claims. While the specification sets forth TRP8 of SEQ ID NO:2 and 4 with calcium and taste modulating activities, such limitations cannot be read into the claims from the specification. Thus, the metes and bounds of the claim recitations remain indefinite to one of skill in the art. As the claims exhibit no structural or functional limitations as to that which constitutes a "TRP8" molecule or it's "activation", any similar molecule with associated activity may meet the claim limitations.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claim 17 is rejected under 35 U.S.C. 102(b) as being anticipated by, Molecular and functional characterization of a novel mouse transient receptor potential protein homologue TRP7. Ca(2+)-permeable cation channel that is constitutively activated and

enhanced by stimulation of G protein-coupled receptor, Okada et al., JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Sep 24) 274 (39) 27359-70. This reference is cited as a 102(b) in view of the effective filing date of 4-13-01 for claim 17 as set forth above.

Prior to setting forth the rejection it is noted that the preamble of claim 17 is deemed to be non-limiting. In particular, the preamble merely recites the purpose of a process or intended use of the TRP8 molecule, and the body of the claim does not depend on the preamble for completeness. Instead the process steps or structural limitations are able to stand alone, see in particular MPEP 2111.02. In particular, the preamble notes the identification of a compound that induces a perception of a bitter taste. However, the body of the claim does not require any step particular to identification of such a compound as identified. Instead the method steps require only contacting and measuring such that increases in the level of activated TRP8 in the presence of a test compound be measured so as to indicate a TRP8 inducer. In effect the steps merely set forth a screening assay for activators or inducers of TRP8. Moreover, none of the steps are deemed to depend on the preamble for completeness as no compound identified by the method is required to be a compound that induces the perception of a bitter taste. Thus, the preamble recitation is non-limiting for the purposes of consideration with respect to the prior art. Amendment of the claim so that the outcome is consistent with the preamble would provide for the recitation to receive patentable weight.

Okada et al., teaches that characterization of mammalian homologues of Drosophila transient receptor potential protein (TRP) are important clues to understand

molecular mechanisms underlying Ca(2+) influx activated in response to stimulation of G(q) protein-coupled receptors in vertebrate cells. Okada isolates cDNA encoding a novel seventh mammalian TRP homologue, TRP7, from mouse brain. TRP7 shows abundant RNA expression in the heart, lung, and eye and moderate expression in the brain, spleen, and testis. TRP7 is recombinantly expressed in human embryonic kidney cells and exhibits distinctive functional features, compared with other TRP homologues. Thus, the TRP7 protein is of the same family as TRP8 and shares common structural and functional features. Therefore the TRP7 molecule is deemed to fall under the TRP8 recitation absent structural or functional limitations to the contrary. Such is a broad but reasonable interpretation as the TRP7 member is encompassed by the genus recitation.

Okada measures the level of TRP7 activation. In particular, "the basal influx activity accompanied by reduction in Ca(2+) release from internal stores was characteristic of TRP7-expressing cells but was by far less significant in cells expressing TRP3, which is structurally the closest to TRP7 in the TRP family. TRP7 induced Ca(2+) influx in response to ATP receptor stimulation at ATP concentrations lower than those necessary for activation of TRP3 and for Ca(2+) release from the intracellular store, which suggests that the TRP7 channel is activated independently of Ca(2+) release. In fact, TRP7 expression did not affect capacitative Ca(2+) entry induced by thapsigargin, whereas TRP7 greatly potentiated Mn(2+) influx induced by diacylglycerols without involvement of protein kinase C. Nystatin-perforated and conventional whole-cell patch clamp recordings from TRP7-expressing cells demonstrated the constitutively activated and ATP-enhanced inward cation currents,

both of which were initially blocked and then subsequently facilitated by extracellular Ca(2+) at a physiological concentration. Impairment of TRP7 currents by internal perfusion of the Ca(2+) chelator 1,2-bis(2-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid revealed an essential role of intracellular Ca(2+) in activation of TRP7, and their potent activation by the diacylglycerol analogue suggests that the TRP7 channel is a new member of diacylglycerol-activated cation channels," see in particular abstract, experimental procedures and results.

Thus, the reference discloses multiple assays in which a TRP8 channel protein is contacted with a test compound or vehicle (negative) control and the level of TRP8 activation (conductance) is measured and compared. For example, diacylglycerol treated samples exhibited an increased level of Mn(2+) influx consistent with indication of a TRP8 inducer. Thus, the reference teachings anticipate the claimed invention.

13. Claim 17 is rejected under 35 U.S.C. 102(b) as being anticipated by, Stimulation of Drosophila TrpL by capacitative Ca2+ entry, Estacion et al., BIOCHEMICAL JOURNAL, (1999 Jul 1) 341 (Pt 1) 41-9. This reference is cited as a 102(b) in view of the effective filing date of 4-13-01 for claim 17 as set forth above.

14.

Prior to setting forth the rejection it is noted that the preamble of claim 17 is deemed to be non-limiting. In particular, the preamble merely recites the purpose of a process or intended use of the TRP8 molecule, and the body of the claim does not depend on the preamble for completeness. Instead the process steps or structural limitations are able to stand alone, see in particular MPEP 2111.02. In particular, the

preamble notes the identification of a compound that induces a perception of a bitter taste. However, the body of the claim does not require any step particular to identification of such a compound as identified. Instead the method steps require only contacting and measuring such that increases in the level of activated TRP8 in the presence of a test compound be measured so as to indicate a TRP8 inducer. In effect the steps merely set forth a screening assay for activators or inducers of TRP8. Moreover, none of the steps are deemed to depend on the preamble for completeness as no compound identified by the method is required to be a compound that induces the perception of a bitter taste. Thus, the preamble recitation is non-limiting for the purposes of consideration with respect to the prior art. Amendment of the claim so that the outcome is consistent with the preamble would provide for the recitation to receive patentable weight.

Estacion et al., teach Trp-like protein (TrpL, where Trp is transient receptor-potential protein) of Drosophila, a non-selective cation channel activated in photoreceptor cells by a phospholipase C-dependent mechanism. The peptide is thought to be a prototypical receptor-activated channel. Estacion notes their previous studies showed that TrpL channels are not activated by depletion of internal Ca2+ stores when expressed in Sf9 cells. Estacion et al., disclose using fura-2 to measure cation influx via TrpL, and cell-attached patch recordings to monitor TrpL single-channel activity directly. The experiments found a thapsigargin-induced increase in TrpL activity in the presence of extracellular bivalent cations, with Ca2+>Sr2+>> Ba2+. The increase in TrpL channel activity was blocked by concentrations of La3+ that completely inhibited

endogenous capacitative Ca2+ entry (CCE), but has no effect on TrpL. Estacion suggests that TrpL exhibits trans-stimulation by cation entry via CCE. TrpL has two putative calmodulin (CaM)-binding domains, designated CBS-1 and CBS-2. Estacion conducted further experiments to determine which site was required for stimulation of TrpL by the cytosolic free Ca2+ concentration ([Ca2+]i). A chimeric construct was created in which the C-terminal domain of TrpL containing CBS-2 was attached to human TrpC1, a short homologue of Trp that is not activated by depletion of internal Ca2+ stores or by a rise in [Ca2+]i. This gain-of-function mutant, designated TrpC1-TrpL, exhibited trans-stimulation by Ca2+ entry via CCE. Examination of CaM binding in gel-overlay experiments showed that TrpL and the TrpC1-TrpL chimera bound CaM, but TrpC1 or a truncated version of TrpL lacking CBS-2 did not. Estacion notes that these results suggest that only CBS-2 binds CaM in native TrpL and that the C-terminal domain containing this site is important for trans-stimulation of TrpL by CCE, see in particular abstract, experimental procedures, figures 1 and 3-4 and results.

The TRPL molecule is of the same family as TRP8. Thus a broad but reasonable interpretation of the claims would include the TRPL molecule within the generic TRP8 recitation, absent defining structural and/or functional limitations to the contrary within the claims. Estacion's experiments note effects in relation to vehicle control experiments. In particular, Estacion notes thapsigarin induced TRPL (TRP8) activation (conductance) as measured by patch recordings noting calcium flux. The level indicates increased activation or flux of ions and thus the thapsigarin in comparison to vehicle control indicates a test compound that is a TRP8 inducer as the

activity in calcium flux was increased in response to stimulation. Thus, the reference teachings anticipate the claimed invention.

Status of Claims

15. No claims are allowed.

16. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
September 30, 2003